

***Aspergillus* in Cannabis:**

Evaluating the Evidence and Crafting Sensible Policies.

Abstract

In recent years, there has been heightened scrutiny of potential contaminants in cannabis, ranging from pesticides and chemical fertilizers to heavy metals and biological hazards. Among these, the presence of fungal entities, particularly the genus *Aspergillus*, which has garnered increased attention due to its association with the cannabis mycobiome — a complex network of over 100 fungal agents identified by the United States National Fungus Collections and Fungal Database referenced by Gwinn et al (2023). Despite their natural association with the cannabis plant, concerns have been raised regarding the possible health implications of these fungi, particularly the spores and mycotoxins they may produce. However, these concerns have not been reflected in the currently available body of research, which demonstrates very few cases of aspergillosis directly attributable to cannabis use. Yet increased scrutiny on this issue is causing a severe financial burden to an already struggling industry.

According to CDC figures, symptomatic aspergillosis in the United States occurs primarily in immunocompromised persons and at a rate of 1 to 2 cases per year per 100,000 people (<https://www.cdc.gov/aspergillosis/statistics/index.html>). Burdensome overregulation of the cannabis industry to only address *Aspergillus* contamination would cost the industry as a whole approximately \$5 billion per year which proportionally is a dramatically higher cost relative to reported rates of infections and risks to address this concern by requiring facilities to retrofit HVAC, additional testing, remediate potentially contaminated products, and decontaminate facilities (Substance Abuse and Mental Health Services Administration, 2023). Conversely, costs are better spent on patient education at the consumer, retail and dispensary level to encourage and recommend immunocompromised patients to **not** use unprocessed products that have a higher risk of contamination.

In the study “Cannabis Use and Fungal Infections in a Commercially Insured Population, United States, 2016” (Benedict et al., 2020), insurance coding data was analyzed to examine a correlation between cannabis usage and fungal infections. The findings of this study, despite relying on an extremely limited subset of 24 non-tobacco smoking cannabis consumers from a cohort of 53,217, have been repeatedly cited by regulatory bodies and proponents of rigorous *Aspergillus* testing as establishing a solid link between cannabis and fungal infections. Yet, the study’s authors concede the limitations of their study reflecting the only true conclusion that more research is needed.

Introduction

The Cannabis Industry Alliance of Oregon (CIAO) formed the Cannabis Science and Research Committee (CSAR) to examine existing research on cannabis-based scientific topics. The committee uses peer-reviewed data to compile evidence-based scientific recommendations for policymakers to help legislators and regulators write industry legislation and policy based on scientific evidence and consumer safety. The committee includes plant scientists, healthcare professionals, and industry and policy experts representing diverse voices and opinions. One of the primary missions is to provide an unbiased review of various aspects of cannabis policies, such as industry worker safety, consumer safety, product safety guidance, and the effects of cannabinoids on health.

This white paper presents science-based evidence through a comprehensive review of the literature, explaining the evidence and clarifying questions of concern to consumers, regulators, and policymakers regarding *aspergillus* and aspergillosis. It is evident that research to date lacks significant data sets, an inability to demonstrate causality, or clear evidence implicating cannabis as a clear threat to developing aspergillosis infections at a rate any higher than exists in everyday life.

There is a clear need for additional, comprehensive research studies to gather more data-driven evidence and develop a compelling rationale for extensive *Aspergillus* testing, contrary to what is being suggested by some industry stakeholders. The findings of this review highlight the importance of a cautious approach to cannabis respiratory delivery methods, particularly in vulnerable populations, but fails to substantiate the broad application of specific microbial testing without more validated, peer-reviewed studies and evidence.

As it is premature to extrapolate broad public health policies from such a limited and restricted data set, there remains a pressing need for more comprehensive and scientifically rigorous research to guide and inform decisions about the necessity and scope of *Aspergillus* testing in cannabis. Current medical advice and standards of care for immunocompromised patients is to avoid smoking any substance. This should be based on well-established and demonstrable medical science rather than a tenuous causal link with cannabis from 0.05% of the subjects of a review study (Benedict et al., 2020).

Regulators often write policies based on the research study "Cannabis Use and Fungal Infections in a Commercially Insured Population, United States" (Benedict et al., 2016), yet the study's primary conclusion was that further research needed to be done.

This study is significantly flawed for many reasons: Reliance on health insurance claims data is inherently limited due to issues with the accuracy of diagnoses, potential coding

errors, and a lack of clinical detail undermining the validity of the results. While the study claims to show an association between cannabis use and fungal infections, it fails to establish any causal link.

The study recognizes its own limitations, as is noted in the conclusion; the analysis overlooks crucial confounding factors, such as the concomitant use of tobacco, which may also contribute to fungal exposure, the underrepresentation of cannabis use in ICD codes casts doubt on the accuracy of identifying cannabis users, and the generalizability to the broader population. Additionally, the lack of thorough assessment regarding immunocompromised status raises questions about the robustness of the conclusions. At the same time, the study fails to consider various methods of cannabis consumption, which would account for varying exposure risks.

The absence of direct evidence linking cannabis use to fungal infections, combined with reliance on diagnosis codes, misclassifying risks, and the inability to limit confounding variables, does not represent the true prevalence of these fungal infections, specifically Aspergillosis and fails to produce any actual causal relationship. Furthermore, the study does not adequately address the possibility of reverse causation, where individuals with existing fungal infections might use cannabis for symptom relief rather than cannabis causing the infections. The study's narrow focus on fungal infections ignores other relevant risk factors and environmental exposures.

Finally, the study's authors recognized the gaps in its validity and generalizability. The author is sure that the only true conclusion is the need for further research, as evidenced by the quote in the conclusion: "Despite the limitations inherent in administrative data and our inability to infer causality between cannabis use and fungal infections, our study adds to emerging evidence about this association"(Benedict et al. 2020). The language of "limitations" and "inability to infer causality" identify this study as less than conclusive and document why this study should not be used by regulators when creating policy.

Understanding *Aspergillus*: its prevalence in the environment and association with cannabis and other agricultural crops

Among the pathogenic *Aspergilli*, *A. fumigatus* is the most ubiquitous in the environment and is the primary cause of clinical aspergillosis, followed by *A. flavus*, *A. niger*, *A. terreus*, and *A. nidulans* (Kwon-Chung and Sugui, 2013). Due to its survivability across many environments, *A. fumigatus* is the most prevalent etiological agent of invasive aspergillosis (IA), a severe and often fatal clinical invasive fungal infection (Kwon-Chung and Sugui, 2013). That being said, while *A. fumigatus* is capable of causing human infection; it is primarily a soil-dwelling saprophyte responsible for decomposing organic

matter, thus playing an essential role in environmental nutrient cycling (Tekaiia and Latgé, 2005).

The presence of fungal contaminants and mycotoxins (toxins produced by some fungi) has been studied extensively in other agricultural crops, such as wheat, corn, and peanuts. Additionally, regulations have been developed to reduce the risks of these contaminants to human health. However, for cannabis, rules to ensure the safety of products for human consumption have been inconsistently applied across various states, particularly concerning microbial contamination, often preceding any research specific to cannabis or cannabis products. State cannabis regulations have vastly different approaches to addressing the issue and the level of required microbial testing.

Research on the cannabis mycobiome, including fungi living normally on healthy plants, is still in its infancy. At this time over 100 different species of fungi have been identified on cannabis inflorescences, primarily via DNA screening techniques that identify microbial DNA present on the plant rather than relying on culture growth and identification (Gwinn et al., 2023). A subset of these fungi are symbionts, growing both on (epiphytes) and within the plant tissues (endophytes) (Punja et al., 2023). Host genetics have been demonstrated to be a significant factor influencing which fungi are present on cannabis plants, with some cultivars showing degrees of susceptibility to multiple species of fungi, including *Botrytis* and *Fusarium* in addition to *Aspergillus* (Punja et al., 2023). So far, several species of *Aspergillus* have been described as epiphytes on cannabis, from spores detected on glandular trichomes and resin (Punja & Ni, 2021), making their abundance in the surrounding environment likely a primary factor in their resulting presence on cannabis inflorescences.

To more easily categorize toxigenic fungi for study and assessment of risk, including those of the genus *Aspergillus* or their byproducts, they can loosely be divided into two categories: “field fungi,” those which can invade a crop and can produce toxins before harvest, and “storage fungi,” those fungal species which grow on dead or dying harvested material. Within the *Aspergillus* genus, *A. flavus* can produce the mycotoxin, aflatoxin, in critical agricultural commodities such as peanuts, corn, and other oil crops. In this context, *A. flavus* is considered a “field fungi,” as it produces aflatoxin during the infection of the living plant, disrupting the plant’s normal physiology and damaging the harvested products, often rendering them harmful or unusable for consumption by humans and livestock. In contrast, members of the genus *Penicillium* are an example of “storage fungi” that produce a different class of mycotoxins called ochratoxins and do so during the drying and processing of certain commodities (Milani, 2013).

In addition to the restrictions posed by the life cycles of these two groups of toxigenic fungi described above, the environmental conditions conducive to their production of

mycotoxins are often much narrower than the conditions required for general fungal growth (Ismaiel and Papenbrock, 2015). While both growth and mycotoxin production have been demonstrated during *in vitro* culturing, there are very few reports confirming either occurrence *in vivo* in cannabis (Gwinn et al., 2023). Based upon research on fungal production of both aflatoxin and ochratoxin in food crops such as peanuts, corn wheat, barley, oats, and soy, we know that optimal temperatures and water activity (a_w) are specifically required for both growth and mycotoxin production (Milani, 2013). Generally, the minimum ecological requirements for the growth of several mycotoxin-producing species of *Aspergillus* are a minimum of 0.82 a_w at 25°C (77°F) or 0.81 a_w with temperatures between 30-37°C (86-99°F) compared to the accepted shelf stable level of 0.65 a_w which is a standard regulatory requirement for cannabis flower and is a standard FDA/USDA requirement of other dried food items. This established maximum limit is far below the levels required for *Aspergillus* fungal growth or mycotoxin production. It thus provides a robust margin of safety for consumers (0.15 - 0.20 a_w lower) at the production level (Milani, 2013).

Currently, there is little research demonstrating comparable phytopathology in cannabis. An abstract of a forthcoming paper was presented at the American Phytopathological Society in Denver (October 2023) entitled “Evaluating the dynamics of aflatoxin biosynthesis by *A. flavus* in hemp (*Cannabis sativa*) flowers and seeds.” In this study, hemp flower/seeds and corn kernels were inoculated with *A. flavus* and assessed over 21 days. Although fungal growth was substantial on both substrates, aflatoxin production in the hemp samples was substantially lower than in the corn samples. The authors concluded that hemp flowers and seeds may not be a favorable substrate for aflatoxin biosynthesis (Marshal et al., 2023). More research is needed to determine the true extent to which both pathogenic and toxigenic *Aspergillus* species associate with and potentially infect cannabis plants and/or harvested products.

Aspergillosis:

Medical Aspergillosis caused by *Aspergillus* Exposure

Aspergillus fungi are widespread and almost unavoidable. They are ubiquitous outdoors in the air, soil, and decaying natural materials, such as compost, live plants, trees, and grain crops (Mayo Clinic Staff, 2018). Recent attention to cannabis use has raised concerns about the potential health risks associated with fungal contamination of cannabis and hemp flowers for consumers, especially in medically fragile and/or vulnerable populations.

While the current review and analysis of existing literature on the presence of *Aspergillus* in the mycobiome of cannabis and hemp flowers have raised questions and

concerns, what is less known is the actual rate of Aspergillosis infections relative to the total cannabis consumer population due to a lack of research on the specificity of this issue. Fungal contaminants, including species of *Aspergillus*, have been examined for their potential health implications on consumers and medical patients; however, these studies are limited and fail to account for variables or alternative causes of the dangerous medical conditions that result from fungal exposures (Benedict et al., 2020).

Everyday exposure to *Aspergillus* is rarely a problem for people with healthy immune systems. Typically, when mold spores are inhaled, immune cells surround and destroy them. In people with a weakened immune system, whether from illness, comorbidities, or those receiving immunosuppressant medications, these patients can have fewer infection-fighting cells, potentially allowing organisms like *Aspergillus* to take hold, invading the lungs and, in the most severe cases, spreading to other parts of the body. For most people, “the local and innate immune response is sufficient to clear the organism without requiring the intervention of an acquired immunity” (Gagneux et al., 2023). Despite the therapeutic benefits of medical cannabis, immunocompromised users can potentially face an increased risk of life-threatening infections like IA if exposed to contaminated cannabis products. Thus, understanding the mycobiome of cannabis and hemp flowers is crucial for ensuring consumer safety and implementing appropriate regulatory safety measures. Recommendations for collaborations to address these concerns are discussed later in this publication.

Invasive Aspergillosis (IA) has three categories of systemic infection: 1) allergic bronchopulmonary aspergillosis, 2) chronic pulmonary aspergillosis, and 3) invasive pulmonary aspergillosis (El-Baba et al., 2020).

Allergic bronchopulmonary aspergillosis primarily affects those predisposed to react to aspergillus, either through an allergic response or disease, such as cystic fibrosis. While allergic forms of aspergillosis are not life-threatening, they could lead to a life-threatening infection in high-risk populations, such as solid organ transplant recipients and those on immune-modulating medications (*Aspergillosis Statistics*, 2019).

Chronic pulmonary aspergillosis typically attacks those with an underlying lung disorder, such as chronic obstructive pulmonary disease (COPD) or lung cancer (El-Baba et al., 2020). Here, we focus on IA since it is the most severe form of clinical aspergillosis, with the most serious complications and outcomes.

IA is a serious fungal infection caused by various species of *Aspergillus*. *It almost exclusively affects immunocompromised individuals, such as those with weakened immune systems due to chemotherapy, organ/stem cell transplantation, or HIV/AIDS* (Nabili et al., 2013). The following provides an overview of IA, including its symptoms, diagnosis, and treatment options.

As noted previously, fungi of the genus *Aspergillus* are abundant and can be found ubiquitously in many environmental settings, surprisingly, the research notes that IA outbreaks of susceptible groups are most often associated with exposure to or presence during hospital construction or renovations (Chazalet et al., 1998). These nosocomial aspergillosis infections are often responsible for the most severe cases of disease compared with those that acquired aspergillosis through exposure to natural environments (Chazalet et al., 1998). Certain environmental conditions that pose a significant threat to immunocompromised individuals undergoing chemotherapy, those diagnosed with HIV, or other immunocompromising diagnoses, which can lead to life-threatening or severe fungal respiratory infections should be avoided (i.e., gardening/composting).

Diagnosis of Invasive Aspergillosis:

IA poses a significant challenge in the management of immunocompromised patients, with high mortality rates associated with delayed diagnosis and treatment.

Diagnosing IA can be challenging due to the nonspecific symptoms and the invasive procedures required to obtain the tissue samples needed for diagnosis and culture confirmation.

The symptoms of IA vary depending on the organs affected but may include (Mayo Clinic Staff 2018):

- Fever, chills
- Respiratory symptoms, hemoptysis, shortness of breath
- Chest pain
- Fatigue, malaise
- Unintentional weight loss
- Headache
- Altered mental status
- Neurological deficits
- Dissemination to the skin causing lesions

Diagnostic methods primarily using chest X-rays and CT scans may reveal characteristic findings such as nodules, cavities, or infiltrations in a patient's lungs. Biopsies obtained via bronchoscopy or other surgical procedures and the direct culturing of a patient's tissue or bodily fluids can allow for the direct visualization of fungal elements upon histopathological examination. However, diagnostics by fungal culture can take two weeks or more, depending on the genus and species. Due to the length of culture methods, DNA testing of patient tissues for microbial pathogens via

molecular methods is becoming commonplace as fewer hospitals rely on fungal culturing due to the associated costs and lack of training, supplies, and space.

- Imaging Studies: Chest X-rays and computed tomography (CT) scans may reveal characteristic findings such as nodules, cavities, or infiltrates.
- Laboratory Tests, including blood cultures and respiratory samples, may be used to identify species of *Aspergillus* through culture growth.
- Tissue biopsy, obtained via bronchoscopy or other surgical procedures, allows for direct visualization of fungal hyphae or fruiting bodies through histopathological examination.
- Additionally, serological tests can detect *Aspergillus*-specific antibodies and antigens in serum or bronchoalveolar lavage fluid, aiding in the diagnosis.

Treatment of Invasive Aspergillosis:

Treatment of IA typically involves antifungal medications such as Voriconazole, the preferred antifungal agent, and supportive care (Mayo Clinic Staff, 2018). Other possible antifungal therapeutics include isavuconazole, posaconazole, and liposomal amphotericin B.

In some instances, surgical intervention is preferred. This treatment path is typically for localized disease infection or when complications such as aspergilloma arise, where removal of infected tissue may be necessary (El-Baba et al., 2020). Additionally, IA can cause the formation of aspergillomas, essentially balls of fungus growing in the lungs, leading to an increased risk of bleeding in these tissues. If these bleeding problems arise, embolization procedures may need to be performed by an interventional radiologist.

Prevention:

Understanding the risk factors, clinical presentation, and management strategies is essential for healthcare providers. Future research focusing on detection and diagnostic methods is warranted to address the evolving challenges posed by this life-threatening fungal infection. Regulatory considerations for monitoring and controlling fungal contamination in not only cannabis products but all agricultural products are essential to protect public health and ensure product safety. Still, they must be based on factual scientific evidence and the reality that *Aspergillus* is everywhere, including the hospitals providing treatment, and rarely causes disease in healthy individuals.

A study by Ruchlemer et al. (2014) has acknowledged there is a definite benefit to people using medical cannabis for a variety of reasons; however, there is a significant risk that an immunocompromised user can develop a life-threatening aspergillosis

infection if fungal contamination exposure occurs and is allowed to progress undiagnosed or untreated. This group reviewed ways to mitigate the risk of infection by sterilizing the flower using three different methods: ethylene oxide gas, plasma, and heat (autoclave). The goal was to see if these methods changed the dynamic of the plant's attributes post-sterilization and if these methods changed the count of potentially unwanted microbes afterward. During the study, there was a reduction in the counts of *Aspergillus*; however, this isn't considered practical in a real-world setting due to cost, access, and likelihood of adherence to this standard of processing for a natural plant. They acknowledge the risk to immunocompromised users but not the practicality or necessity of doing this for all plants on a large-scale operation. However, it should also be noted that not all these methods are considered safe for consumption. Plasma sterilization is considered safe in other countries for water sterilization, but gas sterilization is not considered safe for inhalation post-processing. (Ruchlemer et al., 2014)

Most relevant to this publication, immunocompromised patients who choose cannabis products for therapy or wellness care should avoid combusted/vaporized inhalable cannabis products such as smokable flowers and vaporized cannabis oil concentrates in their therapeutic regime. Immunocompromised patients who require an immediate onset mechanism of action similar to respiratory inhalation, we recommend a metered dose inhaler (MDI) as a safer alternative. Although many concentrates are manufactured using organic solvents that are fungicidal, in the name of caution, immunocompromised patients should abstain from inhalation products and instead opt for topicals, transdermal, tinctures, or oral formulations like edibles or MDIs when necessary.

Essentially, it is impossible to avoid exposure to *Aspergillus* in the normal day-to-day course of life, whether you are gardening in your backyard, visiting the local hospital ER, or using cannabis products. Still, if you have had a transplant, are undergoing chemotherapy, or have an alternate immunocompromising diagnosis, you should try to abstain from places and activities with an increased likelihood of exposure. As such, IA poses a significant challenge in the management of immunocompromised patients, with high mortality rates associated with delayed diagnosis and treatment. Understanding the risk factors, clinical presentation, and mitigation strategies is essential for healthcare providers. Future research focusing on detection and diagnostic methods is warranted to address the evolving challenges posed by this life-threatening fungal infection.

Regulatory considerations for monitoring and controlling fungal contamination in not only cannabis products but all agricultural products are essential to protect public health and ensure product safety. Still, they must be based on factual scientific evidence and

the reality that *Aspergillus* is everywhere, including the hospitals responsible for providing treatment.

Economic Considerations:

As reported by the CDC (<https://www.cdc.gov/aspergillosis/statistics/index.html>, accessed on 10/24/24), symptomatic aspergillosis is uncommon and is estimated to occur primarily in immunocompromised persons at a yearly rate of 1 to 2 cases per 100,000 (0.002%). This includes hospitalizations related to IA in the United States, increasing an average of 3% per year from 2000-2013. In 2014, this translated to nearly 15,000 aspergillosis-associated hospitalizations occurring in the United States, with an estimated *total* cost of \$1.2 billion over 14 years. At this rate, IA has a conservative total incidence rate of less than 0.002% of the U.S. population (at most 0.004% in 2014), assuming a U.S. population of 341 million, and a conservative estimate of 19% (64.79 million) of Americans use cannabis regularly (Substance Abuse and Mental Health Services Administration, 2023). That means the estimated risk to cannabis users of aspergillosis is 0.02%.

In 2022, U.S. growers produced approximately 50 million pounds of cannabis nationally. Testing for *Aspergillus alone* costs an average of \$100. But, requiring growers to test and remediate all cannabis for *Aspergillus* nationwide (legal/regulated market) would mean that the industry would be required to spend approximately \$5 billion per year on:

- Lab testing costs
- Remediation of microbial contaminants prior to sale
- Cleaning of facility
- Preventative maintenance and modifications of facilities
- Waste

We suggest, regulations should reflect economic and clinical realities for the industry and public health rather than be based on incomplete science.

Recommendations to reduce *Aspergillus* Contamination for Growers

Cannabis cultivators can reduce the risk of *Aspergillus* fungal contamination in cannabis by implementing various pre- and post-harvest cultivation practices. Some cultivation practices will benefit by reducing the prevalence of other problematic fungal species associated with potential health concerns, including those contributing to Total Yeast and Mold (TYM) counts.

Because *Aspergillus* thrives at high temperatures and relative humidity, one of the most essential strategies for reducing its prevalence in indoor and greenhouse production is maintaining environmental conditions less conducive to fungal growth. Growers should

utilize appropriate ventilation, air conditioning, and dehumidification equipment that is adequately sized for their growing area. This equipment should be regularly cleaned, maintained, and in good working order.

The microclimate closely associated with the growth of cannabis inflorescences (flowers) is also essential. Cannabis flowers maintain a higher relative humidity and temperature than the local ambient environment in which they're grown (Punja et al., 2023). Adding fans to the growing area to circulate air around maturing flowers has been shown to decrease the temperature and relative humidity within inflorescences and significantly decrease the prevalence of culturable fungi (Punja et al., 2023). Both indoor and outdoor growers can further increase air circulation within the crop by creating an open canopy through pruning, excess leaf removal, and appropriate planting density.

Reducing airborne spores in indoor and greenhouse growing environments can also help prevent fungal contamination in cannabis. Dead leaves on the floor in growing areas have been shown to significantly increase the fungal counts in TYM tests on cannabis flowers (Punja et al., 2023). When these dead leaves were tested, *Aspergillus* was one of the fungal species identified. Both indoor and outdoor growers should maintain a clean growing environment free of leaf litter on the ground, floors, and tables, and they should prune out any dead, dying, or damaged leaves from the plants themselves. Growers using a coco coir growing medium should consider sourcing a product that has been pasteurized, as tests conducted on unopened bags of unpasteurized coco coir revealed the presence of *Aspergillus* fungi, particularly *A. niger*, that have the potential to become airborne (Punja et al., 2019). The presence of airborne fungal spores in indoor growing areas may be further reduced through air purification by installing UV-C lights in HVAC systems and by installing HEPA filters that are regularly inspected and replaced. However, to ensure proper sanitization, any UV light system must be checked periodically to confirm effectiveness. Growing areas and equipment, including dehumidifier motor exhaust vents, should always be thoroughly cleaned and sanitized between crop cycles.

Aspergillus also has the potential to cause post-harvest contamination and degradation in cannabis if proper drying and curing practices are not utilized. Care should be taken while harvesting to avoid unnecessary damage to plant tissues that may encourage microbial growth. Any plant material with visible signs of damage or disease should be removed from the crop and discarded. It is highly recommended that growers use a hang-dry method, where either whole plants or individual branches are hung to dry with the flowers still intact on the stems, in comparison to wet-trim methods, where freshly harvested flowers are separated from the stems and mechanically trimmed before being

dried on screens (Punja et al., 2023). During this study, the wet-trim method produced significantly higher fungal counts in TYM tests of dried cannabis flowers.

The most important factor in preventing *Aspergillus* contamination post-harvest is to reduce the moisture content in drying flowers to a level below that conducive to microbial growth by drying and curing in a clean, climate-controlled room with adequate airflow and dehumidification. Nearly all microbial growth will cease when cannabis is thoroughly dried to a moisture content of 12-14% (water activity of 0.62- 0.7_{aw}) or less (Punja et al., 2023).

Pre-harvest Recommendations:

- Control grow room temperature and humidity using HVAC and dehumidification equipment that is adequately sized for your growing area.
- Use fans to decrease the temperature and humidity in the microclimate immediately surrounding flowers.
- Encourage good airflow within the crop by promoting an open canopy through pruning, removing excess leaves, and planting at an appropriate density.
- Thoroughly clean and sanitize all equipment and all pre and post-harvest production areas between crop cycles.
- Keep areas free from leaf litter on the ground, floors, and tables. Prune out and discard any dead, diseased, or damaged plant material.
- When growing in coco coir, choose a product that has been pasteurized.
- Install HVAC systems' HEPA filters and UV lights to reduce airborne spores.

Post-harvest Recommendations:

- Handle plants gently during harvest to avoid causing damage that may encourage microbial growth. Remove and discard any dead, diseased, or visually damaged plant material.
- Use the hang-dry method for drying plants.
- Dry cannabis in a clean, climate-controlled room with adequate dehumidification and HEPA-filtered ventilation.
- Dry cannabis thoroughly to the moisture content mandated by your local cannabis authority or to 12-14% (water activity 0.62-0.7 _{aw}), whichever is less.

Recommendations for Extractor/Processors

On the one hand, extraction labs, processors, and product manufacturers have less to worry about with fungal contamination as many states do not require solvent-based concentrates to be evaluated for microbial contamination. This is due to the elevated temperatures, the steps taken in the distillation process, and the harsh chemical solvents used in the process, which are toxic to microbial life. In contrast, Rosin presses, which use pressure to squeeze out the cannabis extracts, do not reach high

enough temperatures to kill off bacteria and fungi. For these and manufacturers of edible consumer packaged goods like gummies, it is recommended that a facility follows established quality control guidelines such as the FDA's Guidance document CFR 21 part 111 titled "*Small Entity Compliance Guide: Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements.*" Alternatively, a quality control program such as ISO 9001 would establish the baseline standards required for a manufacturing facility. At its core, these quality control programs focus on a few basic tenets.

- All operations related to the products produced at a facility are governed by written and document-controlled Standard Operating Procedures (SOPs).
- All ingredients and supplies that affect the quality of the products being produced at a facility should have their manufacturer batch/lot numbers tracked for quality assurance.
- The facility has and maintains a documented training procedure for each employee that covers the SOPs and duties.
- All employees show and document an Initial and continuing demonstration of competency (IDOC & DOC) for their duties annually.
- Maintain documented, regularly scheduled cleaning, service, and maintenance of all production areas and equipment.
- "When in doubt, treat it like a commercial-grade kitchen." This means stainless steel surfaces or any other non-porous surface is easily disinfected.
- Experimental studies on X-ray irradiation for decontaminating *Aspergillus* in cannabis flowers have shown promising results in rendering pathogens non-viable. However, further research is needed to understand its impact on product quality, cannabinoid degradation, and safety under real-world manufacturing conditions. (Frink S, Marjanovic O, Tran P, et al. Nov 2022)

Recommendations for Future Policy for Public Safety

This committee has reviewed the applicable research concerning fungal toxins, specifically regarding *Aspergillus* and concluded that more research is needed before definitive conclusions can be made. Within cannabis products, *Aspergillus* fungi are a risk to consumers with a compromised immune system. Medical or adult-use consumers who are immunocompromised should avoid or be counseled against purchasing or using any inhalable cannabis products. Sensible regulations should be narrowly tailored to reflect this reality and not impose unnecessary requirements on cannabis growers and extractors that would burden their already time and cost-sensitive operations or cause product releases to rely on inconsistent and non-repeatable laboratory testing. Regulatory considerations for monitoring and controlling fungal contamination in not only cannabis products but all agricultural products are essential to

protect public health and ensure product safety. But must be based in science and research.

Correlating cannabis use to the development of IA or other *Aspergillus* infections has been minimally studied. Yet, the few studies that have been performed to date show meager rates of disease development, usually associated with other complicating health issues primarily related to those who are significantly immunocompromised.

One of the main goals of legislation and regulation is to promote public health and safety. To protect public safety and increase the level of knowledge and data on this topic, this committee proposes the following actions:

1. Cannabis dispensaries should display an advisory poster on site that includes language that addresses these concerns. It is recommended that the poster should include a QR code connecting the user to a survey where they could voluntarily answer a few simple questions about their knowledge of their immune system risk and cannabis product choices. For example: Was the consumer aware of concerns related to inhaled cannabis for immunocompromised individuals? Did the consumer choose an inhalable cannabis option? If inhaled cannabis was selected, would they be willing to notify a collaborative organization if they developed an adverse respiratory infection?
2. Include a possible safety warning on inhalable cannabis products, such as:

Warning: There is a heightened risk of infection to immunocompromised patients using inhalable cannabis products. Patient discretion is advised.

3. Locally, the industry should collaborate with the regulatory agency in that state as in Oregon with the Oregon Liquor & Cannabis Commission (OLCC) and Oregon Health Authority (OHA) as well as cannabis regulatory agencies nationwide to study this topic further and compile additional data with regards to the testing of products for fungal issues and tracking consumers presenting to healthcare institutions with respiratory fungal infections. Additionally on the federal or national level, a committee or agency should be formed to analyze this and other data that would be collected about cannabis use and program implementation.

Microbial testing, quality control protocols, and decontamination methods should be considered to safeguard consumer health and ensure product safety. Still, those methods must demonstrate consistent effectiveness and a correlation to increased consumer safety.

Summary

As an agricultural product, cannabis inflorescence can be susceptible to fungal infestation and contamination as quickly as hospital ventilation systems, construction sites, soil, compost bins, and any place with the right environmental/climatic conditions. Concerning the majority of the public, interaction with and exposure to commensal fungi and their spores and other microbes is a regular and innocuous occurrence as a part of everyday life with little to no health effect or consequence. It is only for a small number of people with compromised immune systems that these fungal exposures are potentially dangerous.

Individuals who are immunocompromised are usually aware of their medical status due to medical diagnoses and multiple interactions with the healthcare system. As a standard practice, these individuals are given a list of instructions by their healthcare team discussing the dangers and risks they will experience from many diverse types of exposure due to their medical status.

Immunocompromised individuals are regularly informed by their physician that they should wear a mask in public, avoid gardening due to the risk of microbial inhalation, and avoid smoking of any kind, cannabis products notwithstanding, regardless of the therapeutic benefits due to this administration method.

This committee supports a patient's right to choose what they believe is best for their health, and we support the guidance of physicians that immunocompromised individuals should **avoid** smoking of all types, tobacco, cannabis, or otherwise. Though the risk is low, inhaled cannabis has the potential to transmit fungal pathogens that can infect lung tissue. For consumers and users with a healthy immune response, this is rarely dangerous; however, immunocompromised individuals should avoid inhaled cannabis and should discuss cannabis therapy with their healthcare team to determine if cannabis use is safe for them.

Further research is needed to 1) explore alternative strategies for mitigating fungal contamination, 2) identify the actual risk related to inhaled cannabis, and 3) assess the efficacy and feasibility of large-scale cannabis production.

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